



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/655,801	09/05/2003	C. Frank Bennett	ISPH-0771	7114
27180	7590	03/29/2006	EXAMINER	
ISIS PHARMACEUTICALS INC 1896 RUTHERFORD RD. CARLSBAD, CA 92008			MCGARRY, SEAN	
			ART UNIT	PAPER NUMBER
			1635	

DATE MAILED: 03/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/655,801	Applicant(s) BENNETT ET AL.	
	Examiner Sean R. McGarry	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-14 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>9/05/03; 11/22/04</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The preliminary amendment filed 3/16/04 added the limitation "which hybridizes to nucleobases 14 through 177 of 5'-untranslated region of". Applicants amendment points to no support for the specific range now recited. Support for the specific range is not readily apparent from the specification or claims as filed. If applicant believes that the specification and/or claims as filed provide support for the specific range now recited applicant should point to such support with particularity.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over

Ding et al [Neuroscience Letters Vol. 220 :89-92, 1996], Peresleni et al [Am. J. Physiol.

Art Unit: 1635

Vol. 270: F971-977, 1996], and Leeson –Wood et al [Cancer Letters Vol. 147: 163-173, 1999] in view of Nunokawa et al [US 6,203,982] and Bennett et al [US 5,998,148].

The claimed invention is drawn to antisense oligonucleotides targeted to a region identified as nucleotides 14-177 of a 5' untranslated region. Nucleotides 14-177 constitutes essentially the entirety of the 5'UTR of SEQ ID NO:3 (see Table I, for example) and the art is applied as it would relate to Targeting the 5'UTR of SEQ ID NO: 3.

Ding et al disclose a 21mer phosphorothioate antisense oligonucleotide targeted to bases 1-21 of the murine iNOS mRNA and also disclose the administration of the oligonucleotide to SJL/J mice as an animal model for multiple sclerosis via injection with a sterile saline solution.

Peresleni et al. disclose a phosphorothioate antisense oligomer targeted to the 5'UTR/initiation codon/ coding region of human iNOS mRNA and disclose the inhibition of human iNOS in BSC-1 cells (see abstract and page 972, for example).

Leeson-Wood et al. disclose the inhibition of C3H 10T1/2 cells via the administration of 15mer antisense oligomers targeted to iNOS mRNA.

The above references have all taught the implications of iNOS in pathological conditions and the benefits of inhibiting the expression of iNOS in such pathological conditions.

None of the references above have specifically taught antisense oligonucleotides comprising modified sugar moieties or modified bases, chimeric oligonucleotides, or a colloidal dispersion system or targeting a 5'UTR of SEQ ID NO:3.

Nunokawa et al have also taught conditions associated with iNOS and benefits of inhibiting iNOS expression. Nunokawa have taught an iNOS with SEQ ID NO: 3 as an iNOS for inhibition.

Bennett et al have taught general targeting guidelines at columns 3-4, for example. It has been taught to target 5'untranslated regions, start codons, coding regions, and 3'untranslated regions of a desired target, for example. It has been taught in column 5, for example, that antisense compounds are commonly used as research reagents and diagnostics, for example. At column 5 it has been taught that antisense oligonucleotides 8-30 nucleotides in length are particularly preferred. At columns 6-7 it has been taught preferred antisense oligonucleotides contain modified internucleoside linkages including phosphorothioate linkages, for example. At columns 7-8 it has been taught that preferred antisense oligonucleotides comprise modified sugar moieties including 2'-O-methoxyethyl. It has also been taught to modify nucleobases in antisense oligonucleotides at column 8-9 which includes the teaching of 5-methyl cytosine and at column 10 it has been taught chimeric antisense oligonucleotides. All of the above referred to modification are known in the art to provide beneficial attributes to antisense oligonucleotides such as increased hybridization and nuclease protection, for example. At columns 10-24, for example it has been taught numerous "carriers" for antisense oligonucleotides. In Table I it has been taught the successful targeting of those regions taught in columns 3-4 with chimeric phosphorothioate oligonucleotides having 2'-MOE (a 2'-O-methoxyethyl modification).

Art Unit: 1635

Since the prior art has provided ample motivation for targeting iNOS via antisense and the prior has furthermore taught the various modifications recited in the claims, the targeted sequence, and teachings for targeting 5' UTR regions, one in the art would clearly have combined the teaching to make the instant invention. The invention as a whole would therefore have been *prima facie* obvious to one in the art at the time the invention was made.

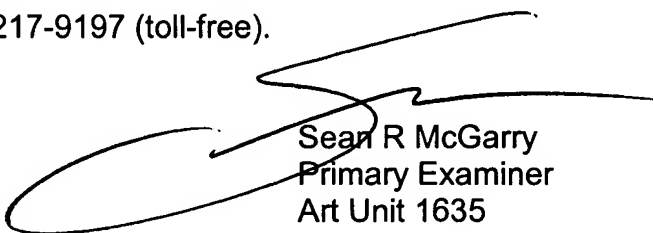
It is noted that SEQ ID NOS: 19-22 were searched to facilitate the search of the region recited and oligonucleotides consisting of such sequences are free of the prior.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R. McGarry whose telephone number is (571) 272-0761. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1635

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Sean R McGarry
Primary Examiner
Art Unit 1635